MENTAL HEALTH SUBGROUP

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Hypothesis #1: Children's risk of developing cognitive, behavioral, and emotional problems are associated with familial psychopathology (e.g. genetics, history of psychopathology) and gene-environmental interactions including those between characteristics of the social environment (e.g. peers, family, community, neighborhood) and exposure to toxins.

A. Gene variations and exposures which affect gene expression affect cognitive, emotional, and behavioral functioning and risk for mental disorders including autism, PDD, schizophrenia, ADHD and depression (risk for suicide).

B. Environmental exposures (e.g. social environment, toxins, etc.) affect early adaptive behavior (i.e. communication, cognitive, motor, social, and activities of daily living (ADL) which predict cognitive, emotional and behavioral functioning across the life span.

Public Health Significance

Prevalence: For children and adolescents age 9-17, the Surgeon General's report on mental health cited studies showing that approximately 20% have a mental disorder with at least mild functional impairment. (Shaffer et al, 1996) and approximately 5 to 9 percent suffer from mental disorders with more severe functional limitations (Friedman 1996), a category classified as "serious emotional disturbance" (SED) (4).

Increased demand for autism-specific services has drawn attention to growing numbers of children with the educational categorization of autism. Epidemiologic studies since 1987 are reporting prevalence rates of about 7.5 per 10,000, on average. These studies report rates of 12.5 per 10,000 for atypical autism/pervasive developmental disorders, for an overall rate of 20 cases per 10,000. Rates for Asperger's disorder are low, 1-2 per 10,000. However, since these studies did not include individuals with less-pronounced variants of autistic spectrum disorder, it is possible that these rates are an underestimate. (NAS 2001)

The percentage of U.S. children ages 6-21 who receive services under the Federal Individuals with Disabilities Education Act (IDEA), Part B for all disabilities combined is 8.92 %. Based on 1999-2000 data, the Office of Special Education reported that 0.74 % of children receive services for emotional disturbance, 1.72% for speech or language impairments, and 0.10% for autism. (US DoE 2000).

Some serious mental illnesses, such as schizophrenia, bipolar disorder, and major depression, generally do not manifest themselves in early childhood. Prodromal symptoms of disease may vary in early life stages and not be recognized until the disease expresses itself overtly, usually in late adolescence or early adulthood. In order to examine the full-range of symptoms that come into play in the development of serious mental disorders, it is necessary to study a large cohort from perinatal exposures forward, in order to have sufficient data to examine gene-environment interactions by ethnicity, gender, and psychosocial stressors.

Morbidity: Twenty-eight percent of U.S. adults, age 18 and over, have an alcohol, drug, or mental disorder (AMD) in a 12-month period.(Regier 1993). The NIMH Epidemiologic Catchment Area Study showed that mental disorders begin much earlier in life than previously thought, indicating the need for longitudinal studies of the mental health of children and youth to track the development of these disorders. Individuals with co-occurring disorders (about 3 % of the population in a 1 year) are more likely to experience a chronic course and to utilize services than are those with one disorder alone.

Quality of life: The extent of AMD disorders indicates that few families in the U.S. are untouched by these disorders. The Global Burden of Disease study revealed that mental illness, including suicide, accounts for over 15 percent of the burden of disease in established market economies, such the U.S. This is more than the disease burden caused by all cancers. Using a measure called Disability Adjusted Life Years (DALYs),

major depression ranked second only to ischemic heart disease in magnitude of disease burden in established market economies. (Murray 1996)

Mortality: Suicide. The strongest risk factors for attempted suicide in youth are depression, alcohol or other drug use disorder, and aggressive or disruptive behaviors. CDC mortality data indicate that suicide was the 3rd leading cause of death among young people 15 to 24 years of age, following unintentional injuries and homicide. The rate was 10.3 per 100,000 or 0.01%. (NIMH)

Economic: Studies report that children's mental health services are fragmented and are difficult to assess. Estimating expenditures is complex, requiring aggregating information across data sources that are not necessarily comparable. Important data relies on regional or state data which is not nationally representative. Also, underreporting of mental health diagnoses in health care claims due to differential coverage for mental health or to perceived stigma associated with mental health service use may underestimate spending. A review of recent national surveys indicated that between 5 and 7 % of all children use any mental health specialty services in a year. The estimate of expenditures for children's mental health care was $11.75 billion (Ringel 2001). A 4-site epidemiologic study found that 21% of youth ages 9-17 received a mental health related service in the past year. (Leaf 1996). Highest rates of mental health specialty care were associated with increased levels of impairment.

Preventability/Malleability: It appears likely that most mental health problems involve a complex mixture of multiple genetic and environmental influences, interacting in nonlinear and nonadditive fashion. Longitudinal designs that allow for relatively long latencies of causal effect are needed to examine the extent to which genetic markers are associated with environmental risk factors to produce disease in the general population. Population data is critical for determining the health policy implications of the newly discovered human gene variants (Eaton 2000). It is critical to understand how risk and resilience processes interact over time in producing different outcomes and the development of psychopathology. This information is needed to design intervention strategies at critical points in a child's life where prevention can most successfully be implemented.

Time sequencing

Assessments during the perinatal period to examine viral, bacterial infections, nutrition, psychosocial stressors, maternal distress, familial history of psychopathology. DNA samples for mother and father should be obtained and banked.

Frequent assessments are recommended during infancy, possibly in 3-month intervals (e.g. 3, 6, 9, 12 months of age), then at key developmental stages (18, 24, 30, 36, 48, 60 months of age) and biennially beginning at age 7.

Need for a Longitudinal Cohort Study

The large cohort NCS study can confer understanding of the development of psychopathology over time and delineate the genetic-environmental interactions that occur. Only a longitudinal study with information on familial psychopathology and genetic material can provide the comprehensive dataset needed to examine the development of physical and mental health conditions over the life course. Additionally, since the trajectory of development for children can be expected to vary by ethnicity, social class, and even region of the country (partly due to variations in clinical practice and access to care), there is need for a wide diversity of participants.

Scientific Merit

The role of genotype in the cycle of violence in maltreated children was the subject of a recent paper published in *Science* (Caspi 2002). This study based on the Dunedin Multidisciplinary Health and Development Study, reported that a polymorphism in the gene encoding the neurotransmitter-metabolizing

enzyme monoamine oxidase (MAOA) was found to moderate the effect of maltreatment. This is the first study to show such a genetic-environmental impact on human development. Eighty-five percent of the males having a low-activity MAOA genotype and who were severely maltreated developed some form of antisocial behavior. Among the males with high MAOA activity, maltreatment did not confer significant risk for conduct disorder.

Understanding the parameters that influence emotional/behavioral outcomes will also guide interventions.

Potential innovations:

Use of the Geographic Information System (GIS) technology for plotting the location of respondents to map prevalence of health conditions geographically and linking this data to other data sources (Census data, TRI, etc) to conduct spatial and correlational analysis. Incorporating Geographic Positioning System technology with GIS can further enhance analysis of environmental conditions for gene-environment interactions in real time sampling situations.

Neuroimaging
Genome
Computer video technology: video conferencing to link subjects with investigators to conduct interviews and follow-ups.

Feasibility

In general, the mental health assessments in the NCS should be administered by personal interviews. These can be done in the home or in clinical settings. In the main, well-trained lay interviewers can be used, but pediatric specialists may be required for specific tests. Some examinations could be done during well-baby and childhood examinations by the family doctor. Some follow-back measures could be obtained by having the respondent mail in questionnaires completed at home.

White Paper is needed to evaluate assessment instruments for outcome measures.

Sampling
Home visits

Measurement
We recommend that a background paper be developed describing the psychometric properties and previous use of outcome measures to assess the development of children's behavioral and emotional functioning at key developmental periods. Workgroup members have suggested the following instruments be included in the review:

Adaptive behavior: Ages and Stages Questionnaire (ASQ), Vineland

Functioning: CAFAS, P-CAFAS, C-GAS

Neurodevelopment: ASQ, DECA, Battelle Dev. Inventory, PENTAB battery

Social development: PENTAB battery, ASQ-SE

Emotional/behavioral development: Children's Behavior Checklist, Strengths and Difficulties Questionnaire with impact and burden extension, B-ITSEA, ASQ-SE

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